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Percutaneous transluminal venous angioplasty in occlusive iliac vein thrombosis resistant to thrombolysis

Systemic thrombolysis is less than optimal in total occlusions of the iliac vein in which patency is 20% or less. We describe an interventional therapeutic procedure that may be effective in such cases. We selected 18 patients (average age, 29.5 years; range, 16 to 71 years) with complete iliac vein occlusion that persisted after 24 to 48 hours of systemic thrombolysis (streptokinase 100,000 U/hr). The ipsilateral femoral vein was punctured, and a guide wire was gently advanced through the thrombus into the inferior vena cava. Multiple inflations were performed with a balloon catheter that was advanced on the wire. A temporary vena cava filter was placed as a protection against possible embolic migration. Systemic thrombolysis was administered for 24 to 48 hours. Control venography and pulmonary angiography were performed. Venography showed good recanalization in seven cases, incomplete recanalization in five cases, and failure in six cases. Patency was maintained for a long time (15.6 months). In conclusion, (1) percutaneous transluminal venous angioplasty is a valuable adjunct to systemic thrombolysis when the latter alone fails; (2) segmental flow and mechanical obstruction were the critical factors, since the pharmaceutical factors were held constant, and (3) a more aggressive incremental interventional strategy warrants consideration. (*AM HEART J* 1993;125:362.)

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Deep phlebitis is responsible for long-term venous sequelae.^{1,2} Such complications are more frequent in cases of proximal phlebitis.³ Systemic thrombolytic therapy in the acute phase restores better venous patency than does administration of heparin.^{4,5}

Nonetheless, 80% of totally occluded iliac clots are resistant to thrombolytic therapy, and the majority of patients with such clots have venous sequelae during follow-up.⁶ Our interventional therapeutic technique combines percutaneous venous angioplasty with thrombolysis in patients with iliac veins in which occlusions persist after thrombolysis.

METHODS

In our unit, patients with proximal deep venous thrombosis of recent onset without contraindication to throm-

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Table 1. Baseline characteristics and clinical course

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Age (yr)	Sex	Cause	Duration of SK therapy		Severity index		Transfusions	Follow-up (mo)	Clinical status	Duplex scan
			Before PTVA (hr)	After PTVA (hr)	Before PTVA	After PTVA				
Group A										
32	F	Surgery	48	36	6	2		28	N	N
71	M	Surgery	24	24	11	3				
25	F	Post partum	48	24	23	2		6	N	N
40	F	Oral contraceptives	24	24	15	8		14	N	—
19	F	Oral contraceptives	24	24	28	9		6	N	N
18	F	Idiopathic	24	24	33	16				
26	F	Idiopathic	48	48	10	0		30	N	N
Group B										
25	F	Surgery	24	24	40	14	+	6	N	N
34	F	Surgery	24	24	24	15				
25	F	Post partum	48	24	20	16	+	6	N	N
22	F	Post partum	24	24	40	32	+	42	N	N
16	F	Post partum	24	24	18	16		6	N	N
Group C										
57	F	Surgery	48	36	40	38		6	Death	
25	F	Surgery	24	24	40	40				
24	F	Surgery	48	24	10	28	+	14	Edema	Occlusion
24	F	Post partum	48	24	40	40		22	Leg ulcer	Occlusion
30	F	Oral contraceptives	24	24	36	36		11	Varicose	Occlusion
19	F	Oral contraceptives	36	24	40	36		12	N	N

SK, Streptokinase; PTVA, percutaneous transluminal venous angioplasty; N, normal.

bolytic therapy and with no apparent cause for early recurrence underwent thrombolysis with streptokinase (100,000 U/hr) for 24 to 48 hours. Ascending venography was performed before and after treatment by injection of contrast medium in the dorsal veins of the feet. If visualization of the iliac vein and vena cava was of poor quality, an iliovenacavography was performed. All patients underwent pulmonary angiography by injection of contrast medium into the main pulmonary artery both before and after treatment. Patients with persistent iliac occlusion at this point were considered to have responded unsatisfactorily to thrombolysis and were selected for treatment with our interventional technique. The biologic efficacy of prior thrombolysis was verified in each case by a plasma fibrinogen level that was persistently below 1 g/L (Clauss method).

Study protocol. A prospective study covered 18 patients (17 women and 1 man; average age, 29.5 years; range, 16 to 71 years). The left iliac vein was affected in 16 cases and the right in two cases. Pulmonary embolism was also present in four cases. Six cases occurred more than 10 days after surgery, and four cases occurred more than 10 days post partum. Four cases occurred while patients were using oral contraceptives, and four were idiopathic (Table 1). The protocol was approved by the University Ethics Committee, and informed patient consent was obtained. Because of concern that a venous clot could be dislodged by the balloon and cause pulmonary embolism, a removable vena cava filter (7F, Prothia, Montrouge, France) was introduced in the inferior vena cava through a brachial vein or

contralateral femoral vein before the procedure according to a technique that has been previously described.⁷ The device consists of a 7F catheter, which is introduced percutaneously. The catheter contains a filter that opens in the vena cava and closes back into the catheter for removal. Streptokinase (100,000 U/hr) was infused through the filter-carrying catheter. Our experience with this device has been reported^{6,7} and now includes more than 250 cases. Immediately after the second phlebography (Fig. 1, A) (24 to 48 hours after the start of streptokinase), the femoral vein ipsilateral to the thrombosis was punctured under fluoroscopic or ultrasonographic guidance with an 18-gauge needle. A 0.035 inch soft-tip guide wire was gently advanced in the inferior vena cava through or along the iliac thrombus. The needle was replaced by a 7F arterial introducer. A brief iliac venography was performed via the side-arm of the arterial sheath. A balloon catheter with an inflated diameter of 10 mm was then advanced over the wire. Multiple inflations along the thrombosed venous segment were performed; in addition, in four cases soft clots were suctioned via a large-lumen 7F catheter; a control angiogram was obtained (Fig. 1, B). When the results were judged to be optimal, the balloon catheter was replaced by a 5F catheter with multiple side holes, which allowed local thrombolytic infusion (streptokinase 50,000 U/hr). The same dose was simultaneously infused through the lumen of the removable filter's carrying catheter. After 24 to 48 hours a third phlebography (Fig. 1, C) and pulmonary angiography were performed, and all catheters were removed. The temporary caval filter was drawn back into its carry-

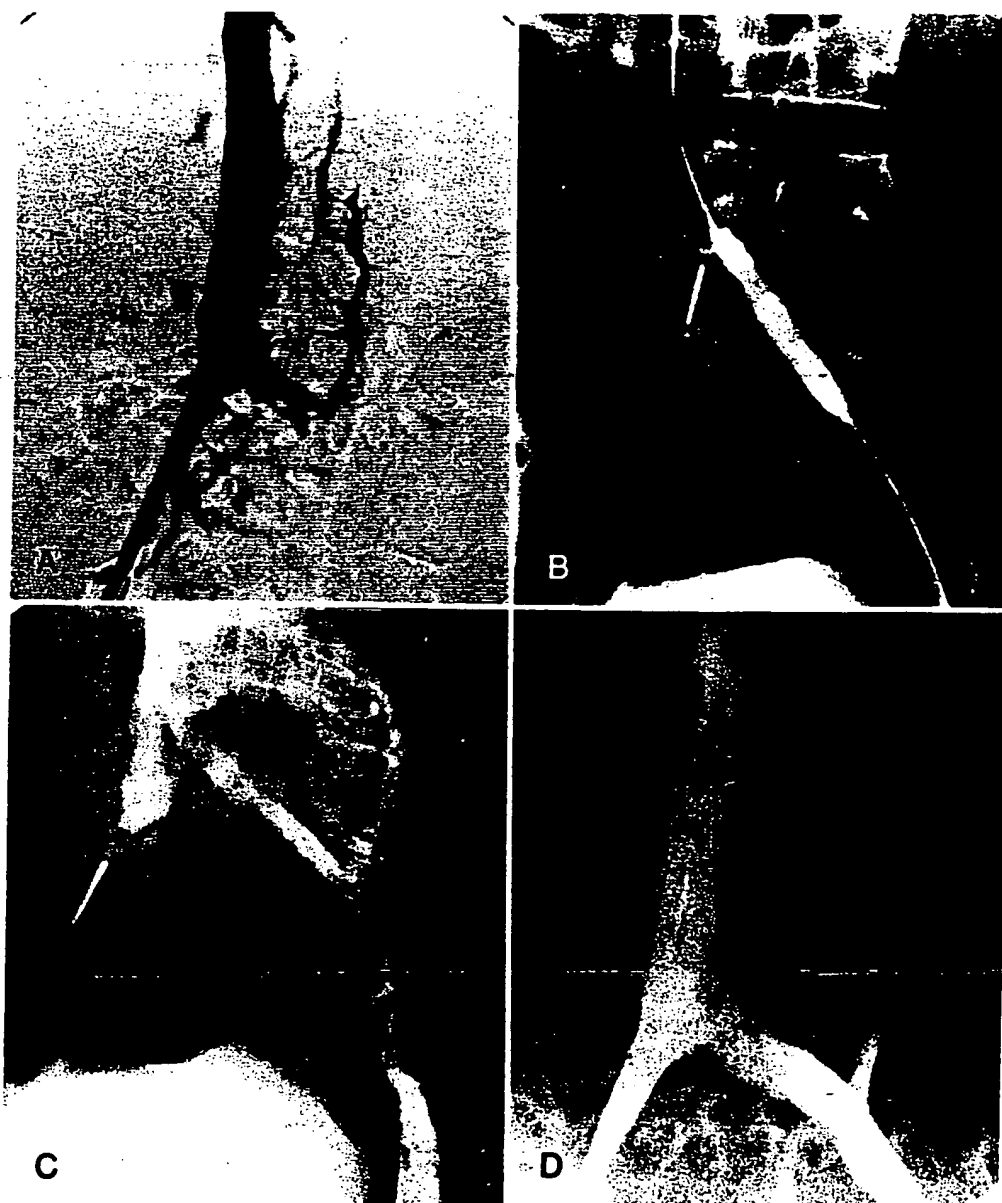


Fig. 1. A, Complete occlusion of the left iliac vein persists after 48 hours of thrombolysis (100,000 U/hr). B, A removable vena cava filter is introduced into the inferior vena cava via the right femoral vein to prevent embolism. Percutaneous venous angioplasty of the thrombosed iliac vein follows. C, After angioplasty the vein is patent, but many filling defects persist. D, After 24 hours of continued thrombolysis the vein appears normal; thrombolysis is stopped and the filter is removed.

ing catheter and withdrawn. The introducers were withdrawn after the fibrinogen level was determined to be >1 g/L. Heparin was administered intravenously for 5 days until fluindione (a vitamin K antagonist) prolonged the prothrombin time to an international normalized ratio of 2 to 3. Fluindione was administered for a period of 6 months.

Venographic score. To allow comparison with previous studies, a severity score⁷ was used to quantify the extension of the venous thrombosis. In summary, the deep veins of the lower limb were divided into five segments (iliac, com-

mon femoral, superficial femoral, popliteal, and calf). Total occlusion and the absence of venous filling were assigned the maximum score (4 points for anterior tibial, popliteal, and common femoral veins; 6 points for posterior tibial, peroneal, and iliac veins; 10 points for superficial femoral veins); segmental occlusion or filling defects were given lower scores. The highest possible score was 40 points for each leg. The venograms and angiograms were subsequently reviewed by an independent panel of three radiologists (Table I).

Follow-up. We limited the patients in the group to 15,

with a follow-up period of more than 6 months; and 13 of these 15 patients were indeed retained in the study. (One was lost to follow-up because of an address change, one died of cancer.) Of the 13 patients studied, 11 underwent a color-coded duplex scan, two underwent a duplex scan and a phlebography, and one patient underwent only a clinical examination.

RESULTS

In three patients, the procedure was unsuccessful because the balloon catheter could not be manipulated across the thrombosed venous segment and into the inferior vena cava because of mechanical obstruction at the junction of the iliac vein and the inferior vena cava. In three patients patency of the iliac vein was achieved, but antegrade flow could not be restored because of persistent thrombosis in the femoral and saphenous veins. In 12 patients the procedure was considered to be successful because antegrade flow was reestablished through the iliac vein. Results of the venography that was performed immediately after the procedure were either entirely normal (one case) or showed filling defects that were indicative of the persistence of clots (11 cases) (Fig. 1, C).

Control venography (Table I). Dramatic improvement was noted in six patients (group A) when normal results of phlebography were achieved or symptoms were limited to the level of the calf veins. In five patients the results were considered to be partially successful (group B): patency of the iliac veins was achieved, but femoropopliteal sequelae persisted. In six patients the procedure failed (group C): no recanalization was achieved in three patients, and in three others reobstruction rapidly followed immediate postprocedural patency without antegrade flow. The venous angioplasty procedure caused migration of clots into the vena cava filter in 16 of 18 cases. The clots that were captured by the filter were dissolved by the continuing exposure to streptokinase. In five cases lysis was not complete at the end of the therapy; in these instances the remaining clots were small and did not prevent the filter from closing into the catheter. In all cases the filter was removed by simple withdrawal through the site of the initial approach. Angiographic control revealed no sign of recurrent pulmonary embolism.

Side effects. Because of local hematomas, which developed at the puncture sites in the groin, four patients needed transfusions of 2 units of blood (three in group B and one in group C). Such bleeding did not result in adverse effects.

Follow-up. Of the 18 patients who were treated, 15 had a follow-up period of 6 months and were retained for the follow-up study; 13 were examined during an average follow-up period of 15.6 months (range, 6 to



Fig. 2. Same patient as in Fig. 1. Follow-up unilateral venography is normal 10 months later.

42 months) five from group A, four from group B, and four from group C. None of the patients in groups A and B had any clinical sequelae. A duplex venous scan was performed in eight of these nine patients. In all cases patency was normal in the venous system of the popliteal veins and in the more proximal deep veins. In two patients partial or total occlusion persisted in the calf veins. In two of the nine patients phlebography was performed and confirmed the patency of the venous system (Fig. 2). Four patients in group C were examined clinically, and three of them had sequelae: leg ulcers in one case, severely varicose veins in one case, and unilateral edema in one case. The fourth patient had no clinical sequelae. A duplex venous scan was performed on four patients. Results were normal in the patient who had no clinical symptoms and revealed complete obstruction of the entire deep venous system in the three others (Table I).

DISCUSSION

Severe trophic venous sequelae constitute frequent and major consequences of deep phlebitis, especially

if the latter is proximal in nature.⁵ The health costs and the socioeconomic consequences are considerable.² Thrombolytic therapy in the acute phase produces better immediate venographic results than treatment with heparin^{4,5}; however, completely occlusive iliac clots are rarely lysed by thrombolytic therapy. In a recent study of 174 patients who were treated with streptokinase (100,000 U/hr) for an average period of 2.8 days, only 20% of occlusive iliac clots were effectively dissolved, and the majority of the patients had long-term venous sequelae.⁶ Similarly, poor results in cases of completely occlusive thrombi have been reported by numerous authors.⁹⁻¹¹ We set out to determine whether these results in a well-defined subgroup could be improved by a more interventional therapeutic strategy. We studied 18 patients with occlusive iliac clots in whom 24 to 48 hours of streptokinase therapy failed. The purpose of the study was to determine whether the mechanical opening of a passageway in addition to streptokinase therapy might produce better results. Venous angioplasty achieved immediate patency in 15 of 18 patients. Of these 15 three experienced loss of patency in spite of postprocedural streptokinase therapy; in these three patients anterograde flow could not be achieved because of persistent distal occlusion. In the 12 other patients iliac patency was maintained. This improvement suggests that total occlusion limits the clinical efficacy of streptokinase. Sufficient plasmin may not be generated in the core of the occluding clot because it is excluded from the circulation and thereby from the thrombolytic agent. Furthermore, continuous lysis and clotting may take place at the inferior extremity of the occluding clot. This vicious circle may be set in motion by the mechanical obstruction to flow of the occlusive thrombus with stasis. The sequence of events in successful recanalization supports this view: percutaneous venous angioplasty restores flow to the iliac vein, but filling defects usually persist (Fig. 1, C); these clots dissolve with continuing thrombolysis once flow has been restored (Fig. 1, D). The three immediate reocclusions also argue in favor of this interpretation: in these three cases, a mechanical obstacle at the junction between the iliac vein and the inferior vena cava could not be crossed by the balloon. Free flow could not be restored along the iliac vein, and reocclusion occurred below the obstacle. This obstacle may be a mechanical compression of the vein by the iliac artery entrapping older or more fibrin-rich clots that are resistant to streptokinase therapy.

Follow-up examinations confirm the importance of achieving iliac patency: of four patients whose iliac veins remained occluded, three had trophic venous symptoms, and ultrasonography confirmed occlu-

sion. On the other hand, no patient in whom patency was achieved had clinical consequences. But the long-term significance of patency of the iliac vein cannot be assessed in this short nonrandomized series. During the venous angioplasty procedure, it is necessary to use a temporary vena cava filter for protection against embolic migration. Thrombotic debris that are generated by the procedure are captured by the filter; the clots are in contact with streptokinase in the circulation and are rapidly dissolved. Any fragments that may remain after the period of streptokinase therapy are easily removed with the filter. The negative aspects of the technique are that it is relatively invasive and that in the setting of active thrombolysis it can cause local hematomas, which may create the need for transfusion. In conclusion, the relatively high success rate of our technique, compared with the poor results of systemic thrombolysis alone in the patient group, makes earlier implementation logical; we are presently performing a randomized study that compares a group treated with this technique to another group treated with systemic thrombolysis alone.

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Contents

February 1993 Volume 125, Number 2, Part 1

- CLINICAL INVESTIGATIONS** Increased production of thromboxane A₂ by coronary arteries after thrombolysis 277
T. G. P. Saldeen, MD, PhD, P. Saldeen, MD, W. W. Nichols, PhD, D. L. Lawson, BS, F. A. Nicolini, MD, and J. L. Mehta, MD, PhD, Gainesville, Fla., and Lund and Uppsala, Sweden
- Influence of thrombolytic therapy on the evolution of baroreflex sensitivity after myocardial infarction 285
Olusola Odemuyiwa, MD, Thomas Farrell, MRCP, Anne Staunton, SRN, James Sneddon, MRCP, Jan Poloniecki, DPhil, David Bennett, MD, Marek Malik, MD, and John Camm, MD, London, England
- Estimation of anterior infarct size with body surface QRST integral maps in the presence of abnormal ventricular activation sequence in dogs 291
Yoshio Ichihara, MD, Makoto Hirai, MD, Hiroshi Hayashi, MD, Yasushi Tomita, MD, Masayoshi Adachi, MD, Akira Suzuki, MD, Makoto Tsuda, MD, Makoto Nagasaka, MD, and Hidehiko Saito, MD, Nagoya, Japan
- Supported angioplasty with synchronized retroperfusion in high-risk patients with left main trunk or near left main trunk obstruction 301
Shinsuke Nanto, MD, Kazuhiko Nishida, MD, Atsushi Hirayama, MD, Masayoshi Mishima, MD, Kazuo Komamura, MD, Masafumi Masai, MD, Tetsuo Sakakibara, MD, and Kazuhisa Kodama, MD, Higashi-osaka, Japan
- Matching based on quantitative coronary angiography as a surrogate for randomized studies: Comparison between stent implantation and balloon angioplasty of native coronary artery lesions 310
Peter P. de Jaegere, MD, Walter R. Hermans, MD, Benno J. Rensing, MD, Bradley H. Strauss, MD, Pim J. de Feyter, MD, and Patrick W. Serruys, MD, Rotterdam, The Netherlands
- Low serum apolipoprotein A-1 level in patients with vasospastic angina 320
Kazuyuki Shirai, MD, Takanobu Nii, MD, Mitsuhide Imamura, MD, Tomoki Kawano, MD, Thukasa Mori, MD, Yoshiyuki Nakashima, MD, Jun Sasaki, MD, and Kikuo Arakawa, MD, Fukuoka, Japan
- Assessment of autonomic nervous activity by heart rate spectral analysis in patients with variant angina 324
Hiroyuki Yoshio, MD, Masami Shimizu, MD, Norihiko Sugihara, MD, Yoshihito Kita, MD, Kuniyoshi Shimizu, MD, Fuyuki Minagawa, MD, Hajime Nakabayashi, MD, and Ryoyu Takeda, MD, Kanazawa, Japan

continued on page 5A

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